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EXAMINER	
HOLLERAN, ANNE L	
ART UNIT	**PAPER NUMBER**
1643	

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09/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/600,129	BACUS ET AL.	
	Examiner	Art Unit	
	Anne L. Holleran	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *1-28 and 35-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. The amendment filed 7/6/2007 is acknowledged. Claims 1-38 are pending. Claims 1-28 and 35-38, drawn to non-elected inventions, are withdrawn from consideration.

Claims 29-34 are examined on the merits.

Claim Rejections Withdrawn:

2. The rejection of claims 29-34 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of treating a subject with cancer that expresses EGFR, does not reasonably provide enablement for treating a subject with any type of cancer regardless of the EGFR status of the cancer is withdrawn in view of the amendment to the claims.

Claim Rejections Maintained:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 29-32 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 29-32 remain rejected under 35 U.S.C. 112, second paragraph, because claim 29 refers to treating a subject with an anti-EGFR antibody when Her3 expression levels are low.

Applicants' arguments have been considered but fail to persuade. The passages in the specification pointed to by applicants refer to an examples of what is considered a low level of expression, but does not appear to define the boundaries of "low level" of expression. Therefore, the metes and bounds of the limitation "when Her3 expression levels are low" are not defined.

4. Claims 30, 32 and 34 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not set forth in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants' arguments have been considered, but fail to persuade. Applicants argue that the examiner has mischaracterized the teachings of US Patent 6,235,883, and that because US Patent 6,233,883 is a US Patent, it is presumed enabled. Therefore, the ABX-0303 monoclonal antibody is enabled, US Patent 6,233,883 teaches ABX-0303.

To the extent that US Patent 6,235,883 does indeed refer to hybridoma E7.6.3, the examiner agrees with applicants. However, it is noted that US Patent 6,235,883 does not claim hybridoma E7.6.3, nor does it claim ABX-0303. Therefore, the examiner has not based the rejection on the assertion that US Patent 6,235,883 fails to enable the hybridoma E7.6.3 or the monoclonal antibody ABX-0303. The passages US Patent 6,235,883 pointed to by applicant teach the amino acid sequences and nucleic acid sequences encoding those amino acid sequences, where the amino acid sequences are those of the variable regions of the heavy and

light chains of the antibody produced by the hybridoma E7.6.3. However, in the instant case, the claims are drawn to methods that require the use of a specific antibody, the monoclonal antibody ABX-0303, which is an antibody that comprises more than the variable regions of the heavy and light chains of the antibody produced by the hybridoma E7.6.3. The disclosure of the US Patent 6,235,883 does not provide the entire sequence of this specific antibody. Additionally, Applicants pointed to the disclosure of Yang (see below under 103 rejections) as evidence that that the production of the ABX-EGF antibody was well known to those of skill in the art. While Yang may show that the antibody exists and is available to certain individuals, the teachings of Yang are not evidence that all restrictions on availability of ABX-EGF have been removed. Therefore, the rejection is maintained because the instant specification does not provide the sequence of the entire antibody and because US Patent 6,235,883 does not provide the sequence of the entire antibody claimed in the instant methods.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 29, 31 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Herbst (Herbst, R.S. et al., Expert Opin. Biol. Ther., 1(4): 719-732, 2001) in view of Xia (Xia, W. et al. Clinical Cancer Res. 5: 4164-4174, 1999).

Applicants' arguments have been considered, but fail to persuade. Applicants are of the opinion that the combination of Herbst with Xia would suggest to one to treat a patient with high levels of EGFR, not a patient with low levels of HER3. However, the rejection is maintained because the claims read on methods of treating a subject "when HER3 expression levels are low", and the claims do not recite a separate step of categorizing patents and then choosing a certain category to treat. As currently recited, the claims are drawn to methods comprising detection of HER3 (which is a step that could also include detecting other HER family members in addition to HER3, such as in the method of Xia) and then treating "when HER3 expression levels are low". Therefore, the method reads on measuring multiple HER family members and then treating a cancer that happens to have low level of HER3, and includes methods where the level of HER3 was not necessarily the deciding factor. The cited prior art teaches comparing levels of expression of EGFR, HER3 and HER2 in oral SCC and head and neck SCC and teaches that in head and neck SCC, HER3 expression levels are low (Xia). Herbst teaches treating head and neck SCC with an anti-EGFR antibody, which happens to be a cancer that has low expression of HER3. Herbst in addition teaches the desirability of targeting head and neck SCC with an anti-EGFR antibody because head and neck SCC has high expression of EGFR. Therefore, Herbst suggests measuring EGFR levels to find those cancers that might be treatable

by anti-EGFR treatments. Thus, it would have been obvious to combine Herbst with Xia, because Herbst teaches targeting EGFR in head and neck SCC and because Xia teaches measuring EGFR (in addition to HER3) and that in head and neck SCC.

6. Claims 29-34 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Herbst (Herbst, R.S. et al., Expert Opin. Biol. Ther., 1(4): 719-732, 2001) in view of Xia (Xia, W. et al. Clinical Cancer Res. 5: 4164-4174, 1999) and further in view of Yang (Yang, X.-D. et al., Critical Reviews in Oncology/Hematology, 38: 17-23, 2001).

Claims 30, 32 and 34 are drawn to methods using an the ABX-0303 antibody (which the specification teaches is also known as ABX-EGF).

The rejection is maintained for the reasons given above for the rejection over the combination of Herbst with Xia.

The combination of Herbst and Xia teach as set forth above for claims 29, 31 and 33. Neither Herbst or Xia teaches methods comprising the use of ABX-0303. However, ABX-0303 appears to be a useful anti-EGFR antibody, because Yang teaches that it is a completely human antibody, and because it completely eradicates a human tumor xenograft (see page 20, section 2.3). Also, Yang teaches that the antibody appears to be useful in xenografts that express high levels of EGFR. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used Yang's ABX-EGF antibody instead of the antibody of Herbst (C225) for the treatment of SCC of head and neck, a cancer that expresses low levels of HER3. One would have been motivated by the teachings of Yang with regard to efficacy of the ABX-EGF antibody and also because the ABX-EGF antibody is a fully human

antibody which lessen the immune response that a human subject would have to the administration of an antibody.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne Holleran, whose telephone number is (571) 272-0833. The examiner can normally be reached on Monday through Friday from 9:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on (571) 272-0832. Any inquiry of a general nature or relating to the

status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Official Fax number for Group 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Anne L. Holleran
Patent Examiner
September 17, 2007

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER